REMARKS

Claims 1, 4, 6-10, 12, 17, 29, 30, 39, 41-46, and 49-68 were pending in this application. Claims 1, 41-44, 49, and 59 have been amended. Upon entry of this Amendment and Response, claims 1, 4, 6-10, 12, 17, 29, 30, 39, 41-46, and 49-68 will be pending upon entry of the instant amendment.

Support for the amendments to claims 1, 6, 41, 43-44, 49, and 59 can be found in the claims as originally filed, and throughout the specification, including at least at page 10, lines 1-2, page 19, lines 17-20 and lines 27-28, and Figures 25 and 26. Support for the amendment to claim 42 can be found throughout the specification, including at least at page 5, lines 24-25.

Claims 1, 41, 43, 44, and 59 have been amended to refer to the corresponding SEQ ID NO provided in the amended sequence listing filed on March 8, 2007. In view of the amendments to claims 1, 41, 43, 44, and 59, Applicants submit that the objection to these claims is overcome.

No new matter has been added. Entry of the replacement sequence listing and claim amendments is respectfully requested. Cancellation of and/or amendments to the claims should in no way be construed as an acquiescence to any of the Examiner's objections and/or rejections. The cancellation of and/or amendments to the claims are being made solely to expedite prosecution of the above-identified application. Applicants reserve the option to further prosecute the same or similar claims in the present or another patent application. The amendments made to the claims are not related to any issues of patentability.

Interview Summary

Applicants' attorneys Debra Milasincic and Cristin Cowles thank Examiner Gussow and Examiner Blanchard for participating in a telephonic interview on June 24, 2008 in which the enablement rejection, including the "portion" language of claim 1, was discussed.

Rejection of Claims 1, 4, 6-10, 12, 17, 28-30, 41-46, and 49-68 Under 35 USC 112, First Paragraph

The Examiner has maintained the rejection of claims 1, 4, 6-10, 12, 17, 28-30, 41-46, and 49-68 under 35 U.S.C. § 112, first paragraph for lack of enablement. Applicants respectfully traverse this rejection.

A. Enablement of claims 41 and 42

The Examiner has rejected claims 41 and 42 for lacking enablement, suggesting that one of ordinary skill would not expect the claimed sequences to function as enhancers in view of the teachings of Wickham *et al.*

Amended claim 41 (and dependent claim 42) is directed to a fusion protein comprising an enhancer sequence comprising an amino acid sequence selected from the group consisting of: YSFE (SEQ ID NO: 5), YSFEDL (SEQ ID NO: 6), and YSFEDLYRR (SEQ ID NO: 9).

Applicants respectfully submit that based on the teachings of the instant specification one of ordinary skill in the art would be able to make and use the claimed peptide enhancer sequences. Examples 6 and 7 and Figures 25 and 26 of the instant specification describe experiments that examine enhancer sequences that are able to increase decabody and peptabody production, respectively. As shown in Figure 25 and 26, Enhancers 2, 4, 8 were able to increase protein production as shown on the Coomassie blue stained gels or Western Blot analysis against the His-tag, respectively. Enhancers 2, 4, and 8 correspond to SEQ ID NOs: 5, 7, and 10, respectively, as described in claim 41. In view of the amendments and the teachings in the specification regarding protein production associated with the claimed enhancer sequences, Applicants respectfully request that the Examiner reconsider and withdraw the 35 USC 112, first paragraph rejection of claims 41 and 42.

B. Enablement of claims 1, 4, 6-10, 12, 17, 28-30, 43-46, and 49-68

The Examiner suggests that one of ordinary skill in the art would not know what portion of the cartilage oligomer matrix polypeptide to use in the claimed peptabody (or monomer thereof). The Examiner further suggests that hinge region of the claimed peptabody (or monomer thereof) lacks enablement because the location of the hinge region is supposedly variable due to the COMP. Finally, the Examiner asserts that the enhancer

sequences of the claimed peptabody (or monomer thereof) lack enablement. Applicants respectfully disagree.

Claim amendments

Amended claims 1 and 44 are drawn to a recombinant peptabody (or monomer thereof) which binds to an epidermal growth factor receptor selected from the group consisting of ErbB-1, ErbB-3, and or ErbB-4, comprising: (a) a cartilage oligomer matrix polypeptide (COMP) portion which is capable of oligomerizing; (b) a peptide enhancer sequence having an amino acid sequence selected from the group consisting of YSFE (SEQ ID NO: 5), YSFEDL (SEQ ID NO: 6), and YSFEDLYRR (SEQ ID NO: 9) and located at the N terminus of the peptabody; (c) a hinge region of an immunoglobulin polypeptide located at the C terminus of the cartilage oligomer matrix polypeptide portion; and (d) an epidermal growth factor receptor ligand which can bind to the epidermal growth factor receptor, located at the C terminus of the hinge region, wherein said recombinant fusion peptabody is capable of inducing cellular death in a cell expressing said epidermal growth factor receptor.

Amended claim 43 describes a peptabody comprising a cartilage oligomer matrix polypeptide (COMP) having a *specific* amino acid sequence, a *specific enhancer sequences* shown by Applicants to increase protein production (as described above), and a hinge region having a *specific amino acid sequence*. More specifically, amended claim 43 is directed to a recombinant fusion peptabody, which binds to the epidermal growth factor receptor ErbB-1 comprising: (a) a human cartilage oligomer matrix polypeptide comprising amino acid residues 16 to 64 of SEQ ID NO: 2; (b) a peptide enhancer sequence for increasing protein production, located at the N terminus of the peptabody and having a sequence selected from the group consisting of YSFE (SEQ ID NO: 5), YSFEDL (SEQ ID NO: 6), and YSFEDLYRR (SEQ ID NO: 9); (c) a hinge region of an immunoglobulin polypeptide comprising amino acid residues 65 to 83 of SEQ ID NO: 2, located at the C terminus of the cartilage oligomer matrix polypeptide; and (d) an epidermal growth factor receptor ligand which binds to the epidermal growth factor receptor and is located at the C terminus of the hinge region, wherein said recombinant fusion peptabody is capable of inducing cellular death in a cell expressing the epidermal growth factor receptor.

Amended claim 49 is directed to an isolated and recombinant fusion peptabody, which binds to an epidermal growth factor receptor selected from the group consisting of

ErbB-1, ErbB-3, and ErbB-4, comprising: (a) a humanized or human cartilage oligomer matrix polypeptide portion which is capable of oligomerizing; (b) a peptide enhancer sequence having an amino acid sequence selected from the group consisting of YSFE (SEQ ID NO: 5), YSFEDL (SEQ ID NO: 6), and YSFEDLYRR (SEQ ID NO: 9) and located at the N terminus of the portion of the cartilage oligomer matrix polypeptide; (c) a hinge region comprising 19 amino acids of an immunoglobulin polypeptide, located at the C terminus of the cartilage oligomer matrix polypeptide portion; and (d) an epidermal growth factor receptor ligand which binds to the epidermal growth factor receptor and is located at the C terminus of the hinge region, wherein said isolated and recombinant fusion peptabody is capable of inducing cellular death in a cell expressing said epidermal growth factor receptor.

Amended claim 59 describes a recombinant fusion peptabody comprising a *specific sequence for the COMP portion, a specific sequence for the enhancer, and a specific hinge sequence*. More specifically, amended claim 59 describes a recombinant fusion peptabody which binds to the epidermal growth factor receptor ErbB-3 or ErbB4 comprising: (a) a human cartilage oligomer matrix polypeptide comprising amino acid residues 16 to 64 of SEQ ID NO: 2; (b) a peptide enhancer sequence for increasing protein production, located at the N terminus of the peptabody and having a sequence selected from the group consisting of YSFE (SEQ ID NO: 5), YSFEDL (SEQ ID NO: 6), and YSFEDLYRR (SEQ ID NO: 9); (c) a hinge region of an immunoglobulin polypeptide comprising amino acid residues 65 to 83 of SEQ ID NO: 2, located at the C terminus of the cartilage oligomer matrix polypeptide; and (d) an epidermal growth factor receptor ligand located at the C terminus of the hinge region, wherein said recombinant fusion peptabody is capable of inducing cellular death in a cell expressing the epidermal growth factor receptor.

The claimed peptabodies of claims 1, 4, 6-10, 12, 17, 28-30, 43-46, and 49-68 each require four elements: a cartilage oligomer matrix polypeptide (COMP) portion, a peptide enhancer sequence selected from the group consisting of SEQ ID NO: 5, 7, or 10, a hinge region, and an EGF ligand *COMP portion.*

With respect to the COMP portion, the Examiner suggests that the "specification does not define the portion of a cartilage oligomer matrix polypeptide (COMP) which is capable of oligomerizing; therefore one of ordinary skill in the art would not know which portion of the polypeptide to use in the peptabody."

First, Applicants respectfully note that amended claims 43 and 59 each require that the COMP region of the peptabody comprise *amino acid residues 16 to 64 of SEQ ID NO: 1*. As such, the COMP region described in claims 43 and 59 is fully enabled, as the claims specify a certain amino acid sequence for this feature.

With respect to amended claims 41, 44, and 49, each of these claims has been amended to specify that the claimed peptabody (or monomer thereof) comprise *a COMP portion which is capable of oligomerizing*. Applicants submit that based on the knowledge in the art at the time of filing regarding the COMP in combination with the teachings of the specification, one of ordinary skill in the art would readily be able to make and use a peptabody comprising a COMP portion which is capable of oligomerizing commensurate with the claims.

In support of Applicants' position that COMP portions that oligomerize were known in the art at the time of filing, Applicants provide herewith references, cited as references C1 to C4 in the enclosed Supplemental IDS, which teach that a COMP portion has to be of a sufficient size in order to have oligomerizing function. In view of the enclosed references that show that COMP portions that oligomerize were known in the art at the time of filing, Applicants respectfully request that the Examiner reconsider the rejection of claims 1, 4, 6-10, 12, 17, 28-30, 43-46, and 49-68 as lacking enablement with respect to the COMP portion.

Enhancer sequence

Independent claims 1, 43, 44, 49, and 59 have each been amended to specify that the peptabody (or monomer thereof) comprise a peptide enhancer sequence having an amino acid sequence selected from the group consisting of YSFE (SEQ ID NO: 5), YSFEDL (SEQ ID NO: 6), and YSFEDLYRR (SEQ ID NO: 9). As described above with respect to claims 41 and 42, the specification provides working examples that show that the claimed enhancer sequences improve protein production of the claimed peptabodies. In view of the amendment, Applicants respectfully submit that the claimed enhancer sequence of the peptabody is fully enabled.

Hinge region

The Examiner also suggests that the "location of the hinge would be different depending upon the portion of the COMP included in the molecule and upon the length of the hinge."

First, Applicants respectfully note that amended claims 43 and 59 both specify that the peptabody comprise a hinge region of an immunoglobulin polypeptide *comprising amino* acid residues 65 to 83 of SEQ ID NO: 2, located at the C terminus of the cartilage oligomer matrix polypeptide portion. In addition, claim 49 requires a hinge region comprising *19 amino acids of an immunoglobulin polypeptide, located at the C terminus of the cartilage oligomer matrix polypeptide portion*. In view of the amendments to claims 43, 49, and 59, Applicants submit that the claims are fully enabled with respect to the hinge region of the peptabody.

Claims 1 and 44 have been amended to describe a peptabody (or monomer thereof) comprising a hinge region of an immunoglobulin polypeptide located at the C terminus of the cartilage oligomer matrix polypeptide (COMP) portion. As such, the hinge described in claims 1 and 44 is located at the COMP portion and the EGF receptor ligand region of the peptabody. Moreover, Applicants submit that one of ordinary skill in the art could make and use the peptabody (or monomer thereof) of claims 1 and 44 without undue experimentation. As described in Applicants' previous response, the specification teaches that the hinge is used as a spacer between protein domains, i.e., between the COMP portion and the EGF receptor ligand of the peptabody (or monomer thereof). The specification provides an example of such a spacer, *e.g.*, a 19 amino acid hinge derived from an Ig. In addition, one of ordinary skill in the art would recognize that the hinge is not limited in sequence and/or length, and, as such, making and using such a hinge would not require undue experimentation.

Based on the teachings in the specification and the knowledge in the art at the time of filing, Applicants submit that claims 1, 4, 6-10, 12, 17, 28-30, 43-46, and 49-68 are fully enabled under 35 USC 112, first paragraph. As such, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

SUMMARY

It is respectfully submitted that this application is in condition for allowance. If there are any remaining issues, or if the Examiner believes that a telephone conversation with Applicants' attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400. Please charge any additional fees or credit any overpayments to our Deposit Account No. 12-0080, under Order No. KZY-002USRCE from which the undersigned is authorized to draw.

Dated: August 18, 2008

Respectfully submitted,

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